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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.

EXAMINER	
ART UNIT	PAPER NUMBER
	6

DATE MAILED:

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Application No.	Applicant(s)
09/396,393	CAPORALETTI ET AL
Examiner	**Art Unit**
Jeffrey Siew	1656

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 July 2001*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *89-102, 116 and 123-129* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *89-102, 116 & 123-129* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

2)☐ Notice of References Cited (PTO-892)

3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s).

DETAILED ACTION

Priority

1. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 89-102,116 & 123-129 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-95 of U.S. Patent No.5,750,497. Although the conflicting claims are not identical, they are not patentably distinct from each other because claims 1-95 of US 5,750,497 are drawn to insulin derivative having the ε-amino group of Lys B29 substituted with an acyl group having at least 10 carbon units which represent a species to the genus claims of instant application which are drawn to insulin derivative substituted with a lipophilic substituent having at least 6 carbon atoms. The species renders the genus obvious.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 89-102,116 & 123-139 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ganong (Review of medical Physiology pps 280-282 1989) in view of Lindsay et al (US3,950,517, Markussen (US5,008,241) and Gammeltoft (Phys. Rev. 6494 pp. 1321-1378 1984).

Ganong et al teach the natural insulin with B3 as ASN (see page 281).

Ganong et al do not teach the limitation of A21 are amino acids other than Lys, Arg, Cys, B1 is Phe , B30 is deleted and ε-amino group of Lys B29 is substituted with an lipophilic substituent having at least 6 carbon units.

Lindsay et al describe methods for reducing the antigenicity of porcine and bovine insuln by acylating the free amino groups at **B1 (Phe),** A1 (Gly) and the amino group of B29 Lys. They teach protection with an acyl group or other blocking group having up to 7 carbon atoms and specifically teach the amino group of **B29 Lys is protected with an acyl group** (see whole doc. esp abstract). They teach that modifications produce a more physiological acceptable derivative that has reduced antigenicity (see abstract).

Markussen et al teach human insulin analogs in which the **Asn is at position A21** (see whole doc esp abstract). They teach that different amino acids at A21 improve the stability of the insulin at acidic pH levels (see abstract).

Marunishi et al teach insulin derivatives in which a fatty acid having 7-21 carbon atoms is attached to amino acid at B1 or B29. They teach modifications produce a pharmacological

Gammeltoft et al teach B23-B30 teach that amino acids B28-B30 are not necessary for biological activity (see p. 1351 4th paragraph) and modifications of the B1 residue do not alter biological character of the insulin (pp. 1327 line 9).

One of ordinary skill in the art would have been motivated to modify Ganong et al insulin by Lindsay et al's acylation in order to make the insulin more physicological acceptable. It would have been prima facie obvious to apply Lindsay et al's modification to Ganong et al's insulin in order to reduce the antigenicity thereby reducing the individual's immunoreactivity to the pharmaceutical insulin while still maintaining its physiological function (see col.3 line 10-25).

Moreover, one of ordinary skill in the art at the time of the invention was made would have been motivated to further modify Ganong's insulin by the teachings of Markussen, Gammeltoft and Marunishi in order to increase the stability, solubility and prolonged activity. It would have been prima facie obvious to apply of Markussen, Gammeltoft and Marunishi modifications to increase the stability of Ganong's insulin for pharmaceutical injections.

4. The response filed 7/9/01 has been fully considered and deemed not persuasive. The response argues that Lindsay et al do not teach deletion of B1. The claims read on the alternative of B1 is Phe or deleted. Lindsay et al teach B1 is Phe.

The response further argues that Markussen et al do not teach B1 is Phe or deleted. The 103 rejection is based on the combination of references and Lindsay et al reference supply the B1 is Phe limitation. Moreover, they argue that Markussen et al teach away from the present

embodiments. They teach a primary A21 substituents-Glu and Asp in which Asp is particularly preferred. While they do additionally teach Lys and Arg as possible residues, their teaching of more preferred substituents does not teach away from using substituents other than Lys and Arg. The response argues that Marunishi do not teach B1 deletion or B30 deleted. The 103 rejection is based on the combination of references. The claims read on the alternative of B1 is Phe or deleted. Lindsay et al teach B1 is Phe and Gammelstoft et al teach that B30 does not have any biological activity.

The response further argues that Gammelstoft et al do not teach limitation of B1 deletion and A21 and B3. . The claims read on the alternative of B1 is Phe or deleted. Lindsay et al teach B1 is Phe. The 103 rejection is based on the combination of references . The claims read on the alternative of B1 is Phe or deleted. Lindsay et al teach B1 is Phe and Gammelstoft et al teach that B30 does not have any biological activity. The response argument that the references do not provide motivation to combine but rather only obvious to try is found unconvincing. The references teach that the modifications would increase stability, solubility of pharmaceutical insulin in a physiological environment. As each of the modification would provide such advantages, one of ordinary skill in the art would have been motivated to perform all modifications to additively increase the stability of the insulin derivative. The rejections are maintained

SUMMARY

CONCLUSION

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is Jeffrey.Siew@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner is on flex-time schedule and can best be reached on weekdays from 6:30 a.m. to 3 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703)-308-1152.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist for Technology Center 1600 whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-3290 and Fax (703) 308-4556 or (703) 308-4242.

Jeffrey Siew

September 19, 2001